

## **AMENDMENTS TO THE SPECIFICATION:**

Please amend from after the third full paragraph on page 4 to before the first full paragraph on page 5 to read as follows:

### **DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS**

[There is provided a] A specific, illustrative enzymatic treatment of retinitis pigmentosa and a kit that includes a pharmaceutical composition for treating the same [in kit form] are provided, according to various aspects of the present invention. More particularly, according to one embodiment of the present invention, [the] one or more selected enzymes ~~employed are glutathione peroxidase (hereinafter referred to as Enzyme A), prolidase (hereinafter referred to as Enzyme B), glucose-6-phosphate-dehydrogenase (hereinafter referred to as Enzyme C), which are administered in accordance with a predetermined time sequence and selected modalities to be described in greater detail below. Preferably, these enzymes include glutathione peroxidase (hereinafter referred to as Enzyme A), prolidase (hereinafter referred to as Enzyme B), glucose-6-phosphate-dehydrogenase (hereinafter referred to as Enzyme C).~~

Please amend page 5, first full paragraph, to read as follows:

Optionally, the treatment [may] also [provide the] uses [of] aldose reductase (hereinafter referred to as Enzyme D), which has been found [to be useful] beneficial

when ~~=as happens in the greater part of cases=~~ the patient complains of visual fogging,  
as often occurs during the course of the disease.

Please amend page 5, second full paragraph, to read as follows:

The enzymes employed in [the] treatments, [in accordance with] according to the present invention, are available [in commerce] commercially in lyophilized form. [and] These enzymes are preferably dissolved in physiological solution in order to [render] make them available in the patient's body upon [for the] treatment.

Please amend page 5, third full paragraph, to read as follows:

Each enzyme – in the form of enzyme solution - is desirably administered by [means of] retrobulbar injection into each eye for three consecutive days, repeating the administration on another two occasions, each separated from its predecessor by a period of one month (for each enzyme). In practice, the procedure is as follows:

Please amend page 5, fourth full paragraph, to read as follows:

- one dose of Enzyme A is injected into the retrobulbar tissue of each eye for three consecutive days at the beginning of [the] treatment, the treatment being [then] repeated in the second and third month;

Please amend page 5, fifth paragraph, to read as follows:

- in the fourth, fifth and sixth month, one dose of Enzyme B is injected into the retrobulbar tissue of each eye for three consecutive days;

Please amend page 5, sixth full paragraph, to read as follows:

- in the seventh, eighth and ninth month, one dose of Enzyme C is injected into the retrobulbar tissue of each eye for three consecutive days;

Please amend page 5, seventh full paragraph, to read as follows:

- if necessary, in the next three months and for three days in each month, the treatment is then continued with Enzyme D, the administration mode being exactly as before.

Please amend from after the seventh full paragraph on page 5 to before the first full paragraph on page 6 to read as follows:

The doses of the various enzymes used [at] for each injection ([for] i.e., in each eye) are as follows:

Enzyme A	0.03 – 0.05 U.I.
Enzyme B	5 – 7 U.I.

Enzyme C	7 – 9 U.I.
Enzyme D	7 – 9 U.I.

Please amend page 6, first full paragraph, to read as follows:

The preferred doses of the various enzymes [at] upon each injection are as follows:

Enzyme A	0.04 U.I.
Enzyme B	6.67 U.I.
Enzyme C	8.00 U.I.
Enzyme D	8.00 U.I.

Please amend page 6, second full paragraph, to read as follows:

Generally speaking, [T]these doses remain the same for all patients, [quite] independently of the typology of the alteration. In particular, the enzyme solutions are prepared [in] such [a way] that the quantities [set out] indicated above may be [contained within] part of an injection of about 0.4 ml of physiological solution. For example, the kit of enzyme solutions suitable for providing injectable doses of about 0.4 ml [containing] with the preferred enzyme quantities [as] set [out] forth above are [to be] desirably prepared as follows:

Enzyme A:

Phial [containing] comprising approximately 10 U.I. of lyophili[s]zed enzyme, [bring] up to about 100 ml [with] in physiological solution.

Enzyme B:

Phial [containing] comprising around 1000 U.I. of lyophili[s]zed enzyme, [bring] up to about 60 ml [with] in physiological solution.

Enzyme C:

Phial [containing] comprising around 2000 U.I. of lyophili[s]zed enzyme, [bring] up to approximately 100 ml [with] in physiological solution.

Enzyme D:

Phial [containing] comprising about 2000 U.I. of lyophili[s]zed enzyme, [bring] up to roughly 100 ml [with] in physiological solution.

Please amend page 6, third full paragraph, to read as follows:

[Naturally] As those skilled in the art will appreciate, these ratios [will have] may need to be modified if [it is decided to change] the dose of any one of the enzymes within its dosing range [as set out above] is changed. The enzymes are desirably administered in the order set forth above, and the injection cycles are to be continued without interruption.

Please amend page 7, first full paragraph, to read as follows:

~~The enzymes are administered in the order in which they are stated above and the injection cycles are to be continued without interruption.~~

Please amend page 7, second full paragraph, to read as follows:

Turning now to [T]the kit used for treating retinitis pigmentos[a]is, in accordance with the present invention, [contains] it includes the aforementioned enzymes in aliquot parts and interactive quantities appropriate for administering:

Please amend page 7, third full paragraph, to read as follows:

a) Enzyme A at a concentration [comprised between] generally within a range of 0.03 U.I. and 0.05 U.I. in about 0.4 ml of physiological solution for three consecutive days, at monthly intervals, for three consecutive days and for each eye;

Please amend page 7, fourth full paragraph, to read as follows:

b) Enzyme B, starting from the month following the last administration of enzyme A, at a concentration [of] between about 5 [to] U.I. and about 7 U.I. in approximately 0.4 ml of physiological solution for three consecutive days, at monthly intervals, for three months and for each eye;

Please amend page 7, fifth full paragraph, to read as follows:

c) Enzyme C, starting from the month following the last administration of Enzyme B, at a concentration generally within a range of 7 U.I. [to] and 9 U.I. in about 0.4 ml of physiological solution for three consecutive days, at monthly intervals, for three months and for each eye.

Please amend page 7, sixth full paragraph, to read as follows:

Optionally, the kit may also [contain] include Enzyme D, to be administered, starting from the month following the last administration of Enzyme C, at a concentration of about 5 U.I. to about 7 U.I. in around 0.4 ml of physiological solution for three consecutive days, at monthly intervals, for three months and for each eye.

Please amend from after the sixth full paragraph on page 7 to before the first full paragraph on page 8 to read as follows:

[In particular] More specifically, the enzymes [are contained in] of each kit are in lyophilized form and in quantities sufficient for at least one complete series of administrations, each enzyme being subdivided into aliquot parts containing a quantity sufficient for one three-month injection cycle, i.e., eighteen injections, or for one daily administration, i.e., two injections, and optionally the appropriate doses of physiological solution [for constituting said] comprising the aliquot parts. In particular, in each kit, the

various enzymes are subdivided into one or more aliquot parts, each [of which contains] comprising, in the preferred dos[ing]age forms [as] set [out] forth above, [from] between about 0.04 U.I [to] and about 0.72 U.I of Enzyme A, from about 6.67 U.I. to about 120 U.I. of Enzyme B, [from] generally within a range of 8 U.I [to] and 144 U.I of Enzyme C and possibly from around 8 U.I to around 144 U.I. of Enzyme D. ~~Possibly there may also be present~~ It is noted that three or more aliquot parts of physiological solution from approximately 0.4 ml to roughly 7.2 ml each may also be present.

Please amend page 8, first full paragraph, to read as follows:

Patients subjected to [the] treatment, in accordance with the present invention, [found] experienced a gradual improvement [of] in their visual acuity and field of vision, colo[u]r perception and image sharpness (definition). Their electroretinograms improved little by little, eventually be[com]ing [reconstituted in the long run] restored over time. The [administered] treatment administered produced a positive response in all [the] patients, albeit over different periods of time. Follow-up checks with the patients after 5-8 years [showed] demonstrated that the [obtained] improvements achieved are [was] permanent and [did] have not [bring out] revealed any side effects [of any kind].

Please amend page 8, second full paragraph, to read as follows:

Some experimental data confirms the hypothesis that retinitis pigmentos[a] is may [could] be due to an enzyme defect that alters the metabolism of the retina, modifying not



only the vision process, but also facilitating [also] the accumulation of pigment[s], [the] a characteristic feature of the illness.

Please amend from after the second full paragraph on page 8 to before the first full paragraph on page 9 to read as follows:

Studies carried out on rabbits (New Zealand/Fulvo di Borgogna) [by one of the applicants] have show[ed]n that [the total] complete inhibition of some enzymes causes variations [of the] in their electroretinograms, with reduction [of] in the depolari[s]zation wave to the point of extinction and [reconstitution] restoration of [the] a normal trace after retrobulbar administration of glutathione peroxidase (Enzyme A) and prolidase (Enzyme B). Erythrocyte level reduction [of] in glucose-6-phosphate dehydrogenase and glutathi-one peroxidase [in] with patients affected by retinitis pigmentos[a]is was [subsequently] demonstrated subsequently by [means of] a comparison of their enzyme erythrocyte concentrations with those of subjects not affected by [this] the illness, seemingly in good health, the two groups being homogeneous [as regards] in sex and age.